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lineage and that such cells form and maintain myelin sheaths. The Examiner further asserts that Webster et al. teach that the administration of growth factors could increase proliferation of progenitor oligodendrocytes, enhance their differentiation, upregulate synthesis of myelin constituents and promote myelin regeneration in adult CNS and consequently, Webster et al. allegedly teach that growth factors with particular biological activities, on the cells that form and maintain myelin sheaths, would be beneficial for treatment of MS. The Examiner acknowledges that "Webster does not teach FGF-9 administration for the treatment of MS", but further asserts that Nakamura et al. teach biological activities for FGF-9 "consistent with" those that would be deemed useful for treatment of MS as identified by Webster et al., and thus, alleges that it would have been prima facie obvious to use FGF-9 for the treatment of MS in view of the teachings of Webster et al. combined with Nakamura et al.

Contrary to the Examiner's assertions and allegations, Applicants assert that Webster et al. teach that fibroblast growth factors such as FGF-2, used for treatment of mature oligodendroglia expressing myelin specific proteins, "failed to induce mitosis and led to the cell death by apoptosis" and consequently, such a fibroblast growth factor "is not able to transform mature, myelin-forming oligodendroglia into large numbers of progenitors that could proliferate, differentiate and produce myelin" (see e.g., page 116, column 2, and more particularly last full paragraph, last 2 sentences, of Webster et al.). Such findings teach that fibroblast growth factors would not be beneficial for the treatment of MS and, therefore, teach away from the use of fibroblast growth factors for the treatment of MS (see also the attached Declaration of Dr. Mitrovic). Further, Applicants assert that Webster et al. teach that "However it is important to note that growth factor-induced responses in human and rodent oligodendroglia differ" and that "in contrast to effects seen in rodent cultures, neither FGF, IGF-I nor PDGF increased proliferation of human oligodendroglia" (see e.g., page 114, paragraph spanning columns 1 and 2, of Webster et al.). Thus, the teachings of Webster et al. teach away from the use of fibroblast growth factors for treatment of MS.

Applicants further assert that Nakamura et al. do not teach "a number of biological activities for FGF-9, including the ability to promote proliferation of primary cortical astrocytes, oligodendrocyte type 2 astrocyte progenitor cells, fibroblasts and neuron-like PC-12 cells" as stated by the Examiner. At most Nakamura et al. examined, by immunohistochemistry and in situ hybridization, the localization of FGF-9 mRNA and protein expression in the rat central nervous system, and do not provide any teachings concerning the biological activity or effect of FGF-9 (see the attached Declaration of Dr. Mitrovic).

Further, Nakamura et al. merely reference the work of Naruo et al. ((1993) J. Biol. Chem. 268(4) 2857-2864) in one sentence stating that "FGF-9 has been shown to promote proliferation of rat primary cortical astrocytes, oligodendrocyte type 2 astrocyte (O-2A) progenitor cells, BALB/c 3T3 fibroblasts, and PC-12 cells (Naruo et al., 1993)" and do not otherwise teach any such biological activity of FGF-9 (see the attached Declaration of Dr. Mitrovic). Naruo et al. merely teach that FGF-9 "stimulated the cell growth of oligodendrocyte type 2 astrocyte progenitor cells, BALB/c3T3 fibroblasts, and PC-12 cells, but not that of human umbilical vein endothelial cells" (column 1, paragraph 1, last sentence). However, it is well known that astrocyte proliferation would not be beneficial for the treatment of MS. Astrogliosis is a major pathological feature of MS and is reportedly responsible for the failure of myelin regeneration and axonal repair in MS lesions (see e.g., Malik et al. (1998) Neuroimmunol. 86(2):155-62; Vawcett et al. (1999)

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Brain Res. Bull. 49(6):377-91). Therefore, Applicants assert that Nakamura et al. do not teach anything about the biological activity or effects of FGF-9 and more particularly, do not teach any biological activity or effect of FGF-9 that would be useful for treatment the treatment of MS.

Therefore, Applicants assert that the use of FGF-9 for the treatment of MS would not have been prima facie obvious in view of the combined teachings of Webster et al. and Nakamura et al. In view the remarks herein and in the Declaration of Dr. Branka Mitrovic, Applicants respectfully request withdrawal of this rejection of Claims 36-41.


CONCLUSION

In view of the foregoing and attached remarks, Applicants believe that the claims are in condition for allowance and that the issuance of a Notice of Allowance is in order.

In the event that there are any questions relating to this application, the Examiner is invited to contact the undersigned patent attorney via telephone, so that prosecution of this application may be expedited.

Respectfully submitted,

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